REMARKS

Claims 1-14, 17-23, 64-76 were pending in the instant application. By this amendment, claims 1, 3-5, 8, 9, 12-14, 17-19, 21, 64, 67-74, and 76 have been amended and new claims 77-112 have been added to clarify the invention, and claims 65 and 66 have been canceled without prejudice to applicants' right to pursue the subject matter of the canceled claims in related applications. In particular, claims 1, 13, 14, 17, and 21 have been amended to specify that the α2M receptor activity is an HSP binding, HSP uptake, or HSP-mediated antigen representation activity, claims 72-74 have been amended to clarify that to "stimulate the activation of cytotoxic T cells" means to "activate cytotoxic T cells," and the amendments to claims 4, 5, 12, 68, 69-74 and 79 have introduced minor changes in the claim language to clarify the invention. In addition, claims 1, 13, and 67 have been amended to delete the recitation of ligand-binding fragments of the α2M receptor, and new claims 77-106 have been added to encompass the subject matter deleted from the amended claims 1, 13, and 67 and claims dependent thereon, and new claims 77-79 and 104 -112 have been added to claim specific preferred embodiments of the invention. Support for the amendments and new claims can be found throughout the specification as originally filed (see, *e.g.*, the specification at page 10, lines 26-34, page 27, lines 20-28; page 32, lines 18-23, page 12, line 32-33). As such, no new matter has been added.

Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

1. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF WRITTEN DESCRIPTION SHOULD BE WITHDRAWN

Claims 1-14, 17-23, and 64-76 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner contends that the specification does not adequately describe the genus of ligand-binding α2M receptor fragments, because, according to the Examiner, one skilled in the art would not be able to envision the detailed structure of fragments of the α2M receptor given the description of the specification. In Section 5 of the Advisory Action dated November 18, 2003 ("the Advisory Action"), the Examiner specifically contends that the multifunctional alpha 2

macroglobulin receptor has many ligand binding domains, and that not all of these domains have been characterized or disclosed in the specification. The Examiner further contends that "the specification has only defined a specific cluster within alpha 2 macroglobulin receptor that binds HSPs and does not define or disclose the broad genus of any and all ligand binding domains found within alpha 2 macroglobulin." Applicants respectfully disagree, for the reasons set forth below.

First, applicants submit that this rejection is in error with respect to claims 68-75 because claims 68-76 do not encompass ligand-binding fragments of the α2M receptor. Therefore, the outstanding rejection of claims 68-75 for lack of written description should be withdrawn.

Second, with respect to the rejection of claims 1-14, 17-23, 64-67, and 76, applicants have amended claims 1, 13, and 67, and claims dependent thereon, *i.e.*, claims 2-12, 14, 17-23, 64-66, and 76, to delete recitation of ligand-binding fragments. Thus, the rejection has been obviated and/or overcome with respect to these claims and should be withdrawn.

Third, claims 77-112 have been added to claim the subject matter encompassing screening methods utilizing ligand-binding fragments of the α2M receptor, including claims 107 to 112, which recite preferred species of ligand-binding fragments of the α2M receptor. Applicants assert that the specification as filed provides adequate written description support for these claimed methods, which do not require a detailed structure of every species of the genus of α2M receptor ligand-binding fragments, for the reasons set forth below.

According to the relevant case law, a claimed genus must be supported by a description of relevant identifying characteristics of a representative number of species. *Regents of University of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), cert. denied 523 U.S. 1089 (1998). What constitutes a "representative number of species" depends upon the knowledge and skill in the art. Moreover, such a description need not be sufficient to provide support to claim each individual species encompassed by the genus. The description is deemed sufficient if it demonstrates to the skilled artisan that the applicant was in possession of the necessary common attributes of the members of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 U.S.P.Q.2d at 1405.

The criteria for determining sufficiency of written description set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description" Requirement" ("the Guidelines") (published in the January 5, 2001 Federal

Register at Volume 66, Number 4, pages 1099-1111), specifies that an applicant may show that an invention is complete by "disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention." (*Id.* at page 1106, column 1, lines 22-33). According to the Guidelines, for each claimed genus, the test requires determination of whether there is sufficient description of

> . . .a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus.
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> *Id.* at page 1106, col. 3, lines 12-29

According to the Guidelines, there are situations where description of even one species adequately supports a genus. "Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (*Id.* at page 1106, col. 3, lines 42-50).

Thus, while applicants agree with the Examiner's assertion in the Advisory Action that there are many ligand binding domains within the multifunctional alpha 2 macroglobulin receptor, all of which may not have not been characterized in the specification, disclosure of each member of a claimed genus is not required by the written description requirement of 35 U.S.C. § 112, first paragraph. According to the relevant case law and the Guidelines discussed above, where the specification discloses any relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics, sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description is misplaced. Here, armed with the description of numerous ligand-binding domain fragments, two specific working examples of ligand-binding α2M receptor sequences, as well as the structural characteristics and functional characteristics of other members of the genus, the skilled artisan would recognize that the applicant was in possession of the necessary common attributes of the genus, *i.e.*, α2M receptor sequences having the ability to bind an HSP, in view of the species disclosed.

Based on the discovery by the applicants that HSPs interact with the α2M receptor, applicants invented the claimed assays which can be used to identify compounds

useful for modulating the immune response. As described in the instant specification, the methods can be carried out with the full-length α2M receptor, or any portion of the α2M receptor that is capable of binding to an α2M-ligand, *e.g.*, an HSP. In this regard, the specification describes both specific structural and functional characteristics and representative species of the genus of ligand-binding fragments of the α2M receptor. For example, at page 12, line 32-33, an 80kDa fragment of the receptor that binds to an HSP is disclosed. The structure of the fragment is described by the exact amino acid residues of the fragment which are highlighted in bold in Figure 8A. Furthermore, at page 3, lines 23-26, cluster regions with binding domains of the α2M receptor are disclosed. In particular, Cluster II is designated as a ligand-binding domain. In addition, at page 4, lines 14-21, ligand-binding fragments are defined based on RAP binding to α2M receptor.

Moreover, the specification provides numerous functional assays that the skilled artisan could use to readily determine additional members of the genus of α2M receptor ligand-binding fragments. In this regard, methods for identifying fragments of the α2M receptor that bind HSPs are described in Section 5.3 (see page 38, lines 13-27) where it is also taught that many of the assays described in Sections 5.2.1 and Section 5.2.2 can be utilized to identify ligand binding fragments of the α2M receptor. For example, in these sections, assays such as *in vivo* binding assays (page 28, line 18 to page 32, line 15), re-presentation assays (page 33, line 35 to page 34, line 9), and CTL assays (page 34, lines 10-29) are described which can be used to test the activity of HSP-binding fragments of the α2M receptor.

Numerous species of the genus of ligand-binding α2M receptor fragments are disclosed in the instant application, *i.e.*, the 80kDa fragment of the α2M receptor, and functional domains of the α2M receptor (see, for example, page 12, lines 27-35 and Figure 8B, and page 48, line 30, to page 49, line 15). In particular, claims 107 to 112 recite specific embodiments of ligand-binding fragments of the α2M receptors which are specifically described and disclosed in the specification of the instant application.

Thus, ligand-binding fragments of the α2M receptor useful in the claimed assays are adequately described in the specification, both structurally and functionally, so that the skilled artisan would recognize that the applicants were in possession of the claimed invention, *i.e.*, assays for identifying compounds that modulate the interaction of an HSP with the α2M receptor.

In light of the foregoing reasons and amendments, Applicants submit the rejection under 35 U.S.C. § 112, first paragraph for lack of written description should be withdrawn.

2. MISCELLANEOUS

Applicants note with appreciation that Section 3 of the Advisory Action indicates that the rejection under § 112, second paragraph, for indefiniteness, has been overcome by the arguments presented in the Remarks section of the Amendment under 37 C.F.R. § 116, filed May 5, 2003.

CONCLUSION

Applicants respectfully request that the present remarks be entered and made of record in the instant application. It is submitted that the foregoing amendments and arguments made herein place the claims in condition for allowance. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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Enclosures